566. *Carbohydrate Derivatives of Alkyl Dithiocarbazinates.*

By R. Hull.

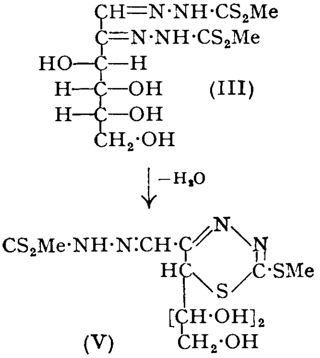
A new series of sugar derivatives is obtained from dithiocarbalkoxyhydrazines (alkyl dithiocarbazinates) (I). The structures of abnormal products obtained from D-glucosamine and D-fructose are discussed.

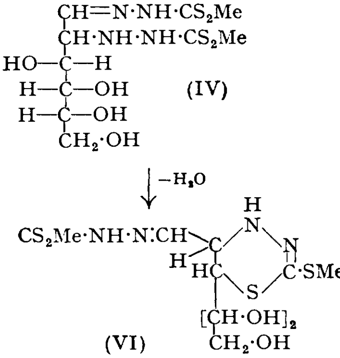
Interaction of dithiocarbomethoxyhydrazine (methyl dithiocarbazinate) (I; R = Me) and aldehydes has been shown to yield derivatives of type (II) (Busch, *J. pr. Chem.*, 1916, **93**, 60). A series of sugar derivatives has now been prepared by using various aldoses and dithiocarbalkoxyhydrazines in aqueous-alcoholic solution. The methyl ester (I; R = Me) gave, in the majority of cases, crystalline products, which would serve as useful derivatives for the identification of the respective sugar. The ethyl ester (I; R = Et) usually gave oils, some of which slowly crystallised, whereas the products from the *iso*propyl ester (I; $R = Pr^i$) remained oils.

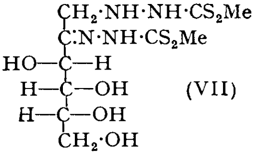
(I) $NH_2{\cdot}NH{\cdot}CS{\cdot}SR$ $R'{\cdot}CH{=}N{\cdot}NH{\cdot}CS{\cdot}SR$ (II)

It appeared that the derivatives have open-chain structures since, in the one case investigated, *N*-dithiocarbomethoxy-*N'*-D-*gluco*pentahydroxyhexylidenehydrazine (II; R = Me, $R' = C_5H_{11}O_5$), the absorption spectrum had maxima and minima similar to those of the ethylidene compound (II; R = R' = Me) and showed no mutarotation.

Similar derivatives have been prepared from D-galactose, L-arabinose, and lactose, and, with the ethyl ester, from D-glucose and D-galactose.


(III) (V)


(IV) (VI)

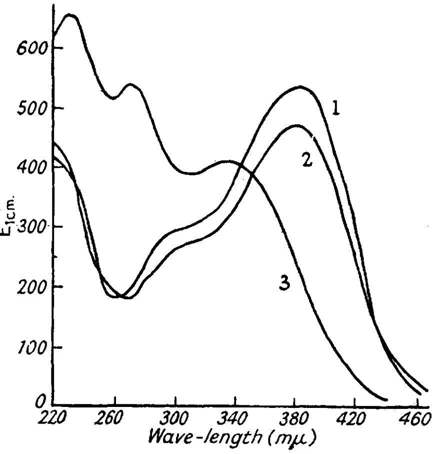

(VII)

Reaction of dithiocarbomethoxyhydrazine with D-glucosamine was abnormal in that two molecular proportions of ester reacted with the sugar. From the analysis the reaction product could be (III) or (IV), the former being obtained by an osazone type of mechanism and (IV) by reaction of a second molecule of the ester with the sugar with elimination of ammonia. The reaction was further complicated in that another molecule of water was eliminated on crystallisation; this could give rise to (V) or (VI) or an anhydro-compound in which water was eliminated from the sugar chain. If (III) was formed by an osazone-type of mechanism, it would be expected that D-glucose and an excess of dithiocarbomethoxyhydrazine would give the same compound: this did not appear to be the case, for only the one condensation product (II; R = Me, R′ = $C_5H_{11}O_5$) was obtained when more than three mols. of ester were used. However, with D-fructose a bis-condensation product was obtained which gave an analysis similar to that of (III or IV) and absorption bands similar to those of (V or VI) but differed markedly in its decomposition point from the D-glucosamine condensation product. It seemed that neither the D-fructose nor the D-glucosamine condensation product contained ethylenic linkages to both $C_{(1)}$ and $C_{(2)}$ of the sugar chain because their absorption bands, which were almost identical (see Figure), differed from that of diacetyl bisdithiocarbomethoxyhydrazone, $[\cdot CMe{:}N\cdot NH\cdot CS_2Me]_2$. It is suggested therefore that the glucosamine and the fructose condensation product are respectively (IV) [giving (VI) on crystallisation] and (VII).

Two molecular proportions of dithiocarbethoxyhydrazine also reacted with one of D-glucosamine, but the product, which was not further investigated, did not lose water on crystallisation.

EXPERIMENTAL

N-*Dithiocarbomethoxy*-N′-D-gluco*pentahydroxyhexylidenehydrazine* (II; R = Me, R′ = $C_5H_{11}O_5$).—(*a*) A mixture of D-glucose (5·1 g.) and dithiocarbomethoxyhydrazine (methyl dithiocarbazinate) (3·4 g.) was heated under reflux in methanol (11·3 c.c.) and water (11·3 c.c.) during 20 minutes. Next morning the solid (7·7 g.) was collected and washed with aqueous alcohol; it had m. p. 117—119°. The *product* crystallised from methanol–water (95 : 5) in colourless needles, m. p. 120—121°, $[\alpha]_D^{20}$ +23·2° (*c*, 4·088 in pyridine) (Found: C, 31·65; H, 5·95; N, 9·0; S, 21·5. $C_8H_{16}O_5N_2S_2,H_2O$ requires C, 31·8; H, 5·95; N, 9·25; S, 21·2%). Light absorption: $\gamma_{\text{max.}}$ 275 mμ (ε, 9541).



1, D-*Glucosamine condensation product in* N/1000-NaOH.
2, D-*Fructose condensation product in* N/2000-NaOH.
3, *Diacetyl bisdithiocarbomethoxyhydrazone in* N/1000-NaOH.

(*b*) D-Glucose (0·9 g.) and dithiocarbomethoxyhydrazine (1·95 g.) in alcohol (2·5 c.c.) and water (3·0 c.c.) were warmed gently during ¼ hour and then set aside for 2 days. The solid (1·5 g.) was collected and after crystallisation from alcohol had m. p. 120—121° alone or mixed with the product from (*a*).

N-*Dithiocarbomethoxy*-N′-L-arabo*tetrahydroxyamylidenehydrazine*.—L-Arabinose (2·9 g.) and dithiocarbomethoxyhydrazine (2·37 g.) were heated under gentle reflux in alcohol (5·5 c.c.) and water (5·5 c.c.) during 20 minutes and then set aside for 2 days. The solid (4·0 g.) was collected and washed with aqueous alcohol. Crystallisation from aqueous methanol gave the *compound* in colourless needles, m. p. 163—164° (decomp.), $[\alpha]_D^{20}$ +15·3° (*c*, 3·006 in pyridine) (Found: C, 33·5; H, 5·95; N, 11·5. $C_7H_{14}O_4N_2S_2$ requires C, 33·1; H, 5·5; N, 11·05%).

N-*Dithiocarbomethoxy*-N′-D-galacto*pentahydroxyhexylidenehydrazine*.—D-Galactose (3·6 g.) and the methyl ester (2·44 g.) in water (8·0 c.c.) and alcohol (7·0 c.c.) gave, as above, the *compound* as colourless needles (from alcohol), m. p. 105°, $[\alpha]_D^{22}$ +16·4° (*c*, 3·016 in pyridine)

(Found : C, 32·95; H, 5·8; N, 9·5; S, 21·6. $C_8H_{16}O_5N_2S_2,0{\cdot}5H_2O$ requires C, 32·8; H, 5·8; N, 9·55; S, 21·8%).

N-*Dithiocarbomethoxy*-N′-(4-β-*galactosyloxy*-D-gluco*tetrahydroxyhexylidene*)*hydrazine*.—Lactose (5·0 g.) and the methyl ester (1·8 g.) in methanol (6 c.c.) and water (12 c.c.) gave, as above, the *product* in colourless needles (from 1 : 1 aqueous methanol), m. p. 165—166° (decomp.) (placed in copper block at 160°), $[\alpha]_D^{22}$ +18·9° (*c*, 3·785 in pyridine) (Found : C, 37·35; H, 5·8; N, 6·3; S, 14·6. $C_{14}H_{26}O_{10}N_2S_2$ requires C, 37·65; H, 5·8; N, 6·3; S, 14·35%).

N-*Dithiocarbomethoxy*-N′-*ethylidenehydrazine*.—Acetaldehyde (1·8 g.) and the methyl ester (4·99 g.) in ethanol (15 c.c.) and water (5 c.c.) were warmed at 40—50° overnight. The solid (1·8 g.) was collected and washed with alcohol. Crystallisation from alcohol (95%) gave colourless needles of N-*dithiocarbomethoxy*-N′-*ethylidenehydrazine*, m. p. 166—167° (Found : C, 32·35; H, 5·5; N, 18·7. $C_4H_8N_2S_2$ requires C, 32·4; H, 5·4; N, 18·9%).

Reaction of D-*Glucosamine with Dithiocarbomethoxyhydrazine*.—D-Glucosamine hydrochloride (6·47 g.) and crystalline sodium acetate (4·08 g.) in water (24 c.c.) were treated with dithiocarbomethoxyhydrazine (7·35 g.) in alcohol (24 c.c.), heated 85° ± 5° during 1 hour, and then kept for 2 days. The *product* (? IV) (3·65 g.), collected and washed with alcohol, had m. p. 187° (decomp.) (Found : C, 31·4; H, 4·7; N, 14·9; S, 32·8. $C_{10}H_{20}O_4N_4S_4$ requires C, 30·95; H, 5·15; N, 14·4; S, 33·0. $C_{10}H_{18}O_4N_4S_4$ requires C, 31·1; H, 4·7; N, 14·5; S, 33·1%). Crystallisation from aqueous 2-ethoxyethanol gave the *tetrahydrothiadiazine* (? VI) as yellow needles, m. p. 198° (decomp.), $[\alpha]_D^{24}$ +417° (*c*, 3·022 in pyridine) (Found : C, 32·4; H, 4·8; N, 14·9; S, 33·9. $C_{10}H_{18}O_3N_4S_4$ requires C, 32·4; H, 4·85; N, 15·15; S, 34·6%).

Reaction of D-*Fructose with Dithiocarbomethoxyhydrazine*.—D-Fructose (0·9 g.) and the methyl ester (1·22 g.) were heated under gentle reflux in alcohol (5 c.c.) and water (1·5 c.c.) during 1 hour. Next morning the *product* (? VII) (0·5 g.) was collected and washed with alcohol. Crystallisation from aqueous methanol gave orange-yellow needles, m. p. 164° (decomp.), $[\alpha]_D^{24}$ +208·4° (*c*, 3·022 in pyridine) (Found : C, 30·4; H, 4·9; N, 14·1. $C_{10}H_{18}O_4N_4S_4,0{\cdot}5H_2O$ requires C, 30·4; H, 4·8; N, 14·15%).

Diacetyl Bisdithiocarbomethoxyhydrazone.—Diacetyl (3·1 g.) and the methyl ester (8·8 g.) were heated in methanol (55 c.c.) and water (15 c.c.) during ½ hour. After a further 3 hours the solid (10·5 g.) was collected and washed with alcohol. The *compound* crystallised from hot dimethylformamide on slow addition of water, in light yellow prismatic needles, m. p. 228—229° (decomp.) (Found : C, 32·6; H, 4·35; N, 18·9. $C_8H_{14}N_4S_4$ requires C, 32·65; H, 4·75; N, 19·05%).

Dithiocarbethoxyhydrazine (I; R = Et).—To potassium hydroxide (22·4 g.) in absolute alcohol (150 c.c.), hydrazine hydrate (70%; 28 c.c.) was added, followed slowly by distilled carbon disulphide (24·4 c.c.), the temperature being kept below 20°. The solid potassium salt was collected, washed with alcohol, and after dissolution in water (200 c.c.) and alcohol (30 c.c.) treated, with shaking, with ethyl bromide (33·8 c.c.) for 2 hours. The oil was extracted with ether and dried, and the solvent removed. The semi-solid material was used as such in the subsequent condensations.

N-*Dithiocarbethoxy*-N′-D-gluco*pentahydroxyhexylidenehydrazine* (II; R = Et, R′ = $C_5H_{11}O_5$).—A mixture of D-glucose (5·15 g.) and the ethyl ester (3·9 g.) was heated under reflux during 10 minutes in alcohol (3 c.c.) and water (3 c.c.), needles contaminated with oily products being formed on cooling. Crystallisation from aqueous alcohol gave the *product* as colourless silky needles (2·7 g.), m. p. 89·5—90·5°, $[\alpha]_D^{20}$ +18·95° (*c*, 3·59 in pyridine) (Found : C, 34·95; H, 6·7; N, 8·75; S, 20·65. $C_9H_{18}O_5N_2S_2,0{\cdot}75H_2O$ requires C, 34·6; H, 6·3; N, 9·0; S, 20·55%).

N-*Dithiocarbethoxy*-N′-D-galacto*pentahydroxyhexylidenehydrazine*.—D-Galactose (2·5 g.) and the ethyl ester (1·9 g.) were heated under gentle reflux during 10 minutes in alcohol (1·5 c.c.) and water (1·5 c.c.). After a long time the *product* (0·8 g.) was collected and crystallised from aqueous alcohol in almost colourless prismatic needles, m. p. 141—142°, $[\alpha]_D^{20}$ +13·8° (*c*, 3·33 in pyridine) (Found : C, 36·4; H, 5·95; N, 9·45. $C_9H_{18}O_5N_2S_2$ requires C, 36·25; H, 6·05; N, 9·4%).

Reaction of Glucosamine with Dithiocarbethoxyhydrazine.—Glucosamine hydrochloride (1·58 g.) and crystalline sodium acetate (1·0 g.) in water (6 c.c.) were treated with a solution of the ethyl ester (2·0 g.) in alcohol (6 c.c.) and heated at 80° ± 5° during ½ hour. On cooling, the yellow *product* (0·7 g.) was collected and washed with aqueous alcohol. Crystallisation from aqueous alcohol gave yellow prismatic needles, m. p. 145—146° (decomp.) (Found : C, 34·7; H, 5·5; N, 13·3. $C_{12}H_{24}O_4N_4S_4$ requires C, 34·6; H, 5·75; N, 13·45%).

*Dithiocarbo*iso*propoxyhydrazine*.—Potassium hydroxide (22·4 g.) in absolute alcohol (80 c.c.) was treated with hydrazine hydrate (70%; 28 c.c.), with stirring. Distilled carbon disulphide (24·4 c.c.) was added during ¾ hour, the temperature being kept below 20°. After 3·5 hours' stirring, the solid potassium salt was collected, washed with alcohol, and dissolved in water (200 c.c.). *iso*Propyl bromide (41 c.c.) was added and the mixture shaken overnight. The oily *ester* was extracted in ether and dried, and the ether removed under diminished pressure. The solid (17·8 g.; m. p. 69—71°) remaining crystallised from benzene in colourless prisms, m. p. 79—80° (Found: N, 18·65; S, 42·8. $C_4H_{10}N_2S_2$ requires N, 18·65; S, 42·7%).

IMPERIAL CHEMICAL INDUSTRIES LIMITED,
RESEARCH LABORATORIES, BLACKLEY, MANCHESTER, 9.

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